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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/056,680

01/25/2002

Teddy Kosoglou

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

HUI, SAN MING R

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/056,680

Applicant(s)

KOSOGLOU ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 is/are pending in the application.
- 4a) Of the above claim(s) 4-10, 12-17, 21-34, 38-41, 46 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 11, 18-20, 35-37, 42-45, and 47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 08262002 08212002 01212003 04212003 05052003 06112003 1032003 12012003
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election of the invention of Group I, claims 1-45 and 47 in response filed September 12, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of specie of blood modifying agent as aspirin, the compound of claim 3, and HMG-Co A reductase inhibitor, simvastatin in response filed September 12, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 46 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in response filed September 12, 2003.

Claims 4-10, 12-17, 21-34, 38-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in response filed September 12, 2003.

Claims 1-3, 11, 18-20, 35-37, 42-45, and 47 have been examined herein to the extent they read on the elected invention and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a composition of treating or preventing the vascular conditions comprising sterol absorption inhibitor, aspirin, and HMG-CoA reductase inhibitors. The specification fails to adequately teach how to use the herein claimed composition to prevent the any vascular event. It is well-known in the state of the art that vascular conditions encompass various cardiovascular disorders such as hypertension, acute myocardial infarction, unstable angina, endocarditis, and even arrhythmia, such as ventricular fibrillation. These conditions are caused by various etiologies. See, Merck Manual, 16th ed., 1992, page 365-367, table of content for cardiovascular disease. Please note that even a basic reference, such as Merck Manual, has over 200 pages of information with regard to cardiovascular disease. The instant claims are so broad that it encompasses the method of preventing **all** vascular disorders. The current known treatments of these disorders depends on the patient populations and the severity of the disorders. Some of the disorders, such as primary

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hypertension, have no known etiology (See Merck manual, page 413). Thus, it is clear from the evidence of the Merck Manual that the ability to prevent vascular condition is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence such as working examples that their claimed invention is indeed useful as preventive for the first occurrence of vascular condition and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claims 1, 11, 18-20, 35-37, 42-45 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the sterol absorption inhibitors recited in claims 2-10, does not reasonably provide enablement for other sterol absorption inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,

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- 3) the presence of absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art
- 7) the predictability of the art, and
- 8) the breadth of the claims.

Applicant fails to set forth the criteria that define "sterol absorption inhibitors ".

There is no physical, chemical, or biological information as to how to elect the suitable sterol absorption inhibitors. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "sterol absorption inhibitors" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. Because of the lack of information and guidance from the instant specification, one of skilled in the art would be required to assess each embodiment individually for physiological activity. The instant claims read on all "sterol absorption inhibitor(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 11, 18-20, 35-37, 42-45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (EP 0720 599, reference CA from IDS received January 21, 2003), and Ullah (WO 99/47123 from IDS received January 21, 2003) in view of Frei (Proc Soc Exp Biol Med. 1999 Dec; 222(3): 196-204).

Rosenblum et al. teaches a composition comprising the compound of Formula (II), lactose, and magnesium stearate (See particularly claims 8, and 9, page 24, example 6, page 29, Examples A and B). Rosenblum et al. also teaches the active compounds therein, including the racemic mixture of compound of Formula (II), can be formulated into a tablet (See Example A and B in page 29). Rosenblum et al. also teaches the effective dosage of compound of Formula (II) as 5 to 1000mg per day (See page 17, paragraph 0065). Rosenblum et al. also teaches the active compounds therein can be combined with HMG-CoA reductase inhibitors, preferably simvastatin, for

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reducing cholesterol and the risk of arteriosclerosis (See 5, paragraph 0028, also claims 16 and 17).

Ullah teaches a composition comprising statins, such as simvastatin, in combination with aspirin, for cholesterol lowering and treating or reducing the risk of developing atherosclerosis (See the abstract, also page 1, lines 14-18). Ullah teaches the dosage for aspirin as 50-650mg (See page 5, lines 34-37).

The primary references do not expressly teach the composition comprising the compound of formula (II) herein, aspirin, and simvastatin together. The primary references do not expressly teach antioxidants be incorporated into the composition containing compound of formula (II) herein, aspirin, and simvastatin.

Frei teaches antioxidants, such as vitamin C and vitamin E, as useful in inhibit the atherogenesis and normalize the vascular functions (See the abstract, page 198, col. 2, second paragraph, also page 199, col. 1, second paragraph, page 201, col. 2, first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the compound of Rosenblum into the composition of Ullah. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate antioxidant into the composition containing compound of formula (II) herein, aspirin, and simvastatin.

One of ordinary skill in the art would have been motivated to combine the compound of Rosenblum into the composition of Ullah. Combining composition of Rosenblum and that of Ullah, which are known to be useful to reduce cholesterol level

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and the risk of atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

One of ordinary skill in the art would have been motivated to incorporate antioxidant into the composition containing compound of formula (II) herein, aspirin, and simvastatin. Vitamin C, an antioxidant, is known as useful to inhibit the development of atherosclerosis. Combining vitamin C with composition containing compounds of Rosenblum and Ullah, which are known to be useful to reduce cholesterol level and the risk of atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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A handwritten signature in black ink, appearing to read 'San-ming Hui', written in a cursive style.

San-ming Hui
Patent examiner
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